AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions, and listings, of claims in this application.

1. (Original) Method of purifying an antibody, preferably an IgG antibody, comprising the steps of:

    1. Purifying an antibody by means of protein A affinity chromatography wherein the protein A is a native protein A or a functional derivative thereof,

    2. loading the thus purified antibody comprising antibody aggregate and protein A or protein A derivative onto an ion exchange material under conditions which allow of binding of the contaminating protein A or its functional derivative to the ion exchanger material and which conditions further allow of resolution in the flow-through of antibody aggregates from antibody monomer which monomer is not complexed with protein A or protein A derivative by means of fractionation of the flow-through, and further

    3. fractionating the flow-through and harvesting from the flow- through of the ion exchanger at least one antibody monomer fraction having both reduced contents of protein A or protein A derivative and further reduced contents of antibody aggregate as compared to the composition of antibody as loaded onto the ion exchange material before.

2. (Currently Amended) Method according to claim ~~2~~ 1, characterized in that the protein A is a recombinant protein A that is engineered such as to allow of single-point attachment to a column material.

3. (Original) Method according to claim 2, characterized in that the recombinant protein A comprises a cysteine in its amino acid sequence.

4. (Original) Method according to claim 3, characterized in that the cysteine is comprised in a segment that consists of the last 30 Amino acids of the C-terminus of the amino acid sequence of the recombinant protein A.

5. (Original) Method according to claim 3, characterized in that the recombinant protein A is attached by at least 50 % via a thioether sulphur bond to the chromatographic support material of the protein A affinity chromatography.

6. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the protein A or its functional derivative is reduced to a concentration of < lng/mg IgG in the flow-through of the ion-exchanger.

7. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the monomericity of the antibody harvested is at least 99% and is achieved by fractionating the antibody peak of the flow-through into at least two fractions and wasting the tail fraction.

8. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the antibody is a monoclonal antibody, preferably an IgG antibody wherein the IgG antibody may be chimeric or CDR-grafted IgG antibody.

9. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the antibody is harvested from a cell culture prior to purifying the antibody by means of protein A affinity chromatography.

10. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the antibody is harvested from a mammalian cell culture.

11. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the antibody that is to be purified by means of protein A affinity chromatography is not treated as to inactivate proteases, preferably is not in admixture with at least one protease inhibitor.

12. (Currently Amended) Method according to ~~one of the preceding~~ claims 3, characterized in that the protease inhibitor is selected from the group consisting of PMSF, a proteinase inhibiting peptide, e-caproic acid, and a reducing sulfhydryl compound.

13. (Original) Method of purifying a product protein, comprising the steps of:

1. loading a solution comprising product protein which product protein comprises monomelic and aggregated forms of said protein onto an ion exchange material under conditions which allow of resolution in the flow- through of said product protein aggregates from said product protein monomer which monomer preferably is not further complexed with a second protein ligand, by means of fractionation of the flow-through and further

2. fractionating the flow-through and harvesting from the flow-through of the ion exchanger at least one product protein monomer fraction having reduced contents of product protein aggregate as compared to the composition of product protein loaded onto the ion exchange material for purification.

14. (Original) Method according to claim 13, characterized in that fractionation is achieved by fractionating or splitting the product protein peak of the flow-through into at least two

fractions and wasting the tail fraction and that, preferably, the monomericity of the antibody harvested is at least 99%.

15. (Currently amended) Method according to claim 12 ~~or 13~~, characterized in that at least one second fraction having a lower degree of monomericity of product protein than the first one is discarded based on the assessment of monomericity.

16. (Original) Method according to claim 15, characterized in that at least one buffer is used for loading and rinsing the ion exchanger which at least one buffer coming off the ion exchanger is constituting the flow-through comprising the product protein peak.

17. (Original) Method according to claim 16, characterized in that the pH of said buffer is set at a pH which is the pi or average pi of the product protein monomer sought to be purified in the range of ± 0.5 pH units around said pi.

18. (Original) Method according to claim 16, characterized in that the pH of said buffer is set at a pH different from the the pi or average pi of the product protein monomer sought to be purified and which pH further vests the product protein monomer with a surface charge which charge leads to ionic attraction in between product protein monomer and the charged groups of the ion exchange material when exposed to or submerged in said buffer.

19. (Original) Method according to claim 18, characterized in that in case of a cation exchanger, the pH of the buffer is set at a value below the average pi of the product protein monomer sought to be purified, preferably set at a value of from 0.5 to 3 pH. units below said average pi.

20. (Original) Method according to claim 18, characterized in that in case of an anion exchanger, the pH of the buffer is set at a value above the average pi of the product protein monomer sought to be purified, preferably set at a value of from 0.5 to 3 pH units above said average pi.

21. (Original) Method according to claim 13, characterized in that said conditions are non-binding conditions as regards binding of the product protein monomer to the ion exchange material such as that consequently more than 70% (w/w) , more preferably more than 80% (w/w) of the product protein loaded onto the ion exchange material can be recovered in the flow-through from the ion exchange material.

22. (New) Method according to claim 13, characterized in that at least one second fraction having a lower degree of monomericity of product protein than the first one is discarded based on the assessment of monomericity.